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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/502,698	02/11/00	FUNAHASHI S	06501-056001

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Janis K. Fraser
Fish & Richardson P.C.
225 Franklin Street
Boston MA 02110-2804

EXAMINER	
MERTZ,P	
ART UNIT	PAPER NUMBER
1646	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/502,698	Funahashi et al.
Examiner	**Art Unit**
Prema Mertz	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 28, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above, claim(s) *6-34* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-5* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3

18) ☒ Interview Summary (PTO-413) Paper No(s). 8

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I (claims1-5) in Paper No. 10 (6/28/01) is acknowledged. The traversal is on the ground(s) that Group II (claims 1-5) drawn to a polypeptide of SEQ ID NO:2, is a subsequence of Group I (claims 1-5) drawn to a polypeptide of SEQ ID NO:1. Thus a prior art search of SEQ ID NO:1 would reveal art for SEQ ID NO:2. This argument is found persuasive and both SEQ ID NO:1-2 will be examined in the instant application.

Claim Rejections - 35 USC § 101

2. Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The instant application has provided a description of isolated proteins. The instant application does not disclose the biological role of these proteins or their significance.

It is clear from the instant specification that the claimed proteins are what is termed "orphan proteins" in the art. An "orphan protein" is a protein whose cDNA has been isolated because of its similarity to known proteins. It is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors (Doerks et al. 1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al., page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-

annotation errors in the sequence databases (Doerks et al. Page 250, column 1, third paragraph). There is little doubt that after complete characterization, these proteins will probably be found to have a patentable utility. The numerous uses of the claimed invention (pages 19-26), are not specific, substantial or credible utilities because Applicants have failed to disclose which other proteins the instant proteins interacts with. Furthermore, since the instant proteins having PDZ domains have not been shown to be involved in the binding of specific proteins, have not been shown to be a disease markers, have enzymatic activities or to be involved in a physiological process that one would want to manipulate for clinical effect, such as regulate respiration, blood pressure, digestion, muscle relaxation, or neurotransmission, the instant specification does not disclose a "real world" use for the claimed proteins, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful. Furthermore, because the claimed invention is not supported by a specific asserted utility for the reasons set forth above, credibility cannot be ascertained.

There is little doubt that, after complete characterization, the claimed proteins will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicants claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966)*, in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all

chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the Court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The Court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to proteins of as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the proteins identified in the specification as proteins having PDZ domains, the instant invention is incomplete. The DNAs of the instant invention and the proteins encoded thereby are compounds which are known to be structurally analogous to proteins which are known in the art as proteins having PDZ domains and which interact with proteins having hydrophobic amino acids at their C-terminal ends (page 5, lines 26-30). In the absence of a knowledge of the natural ligands or biological significance of these proteins, there is no immediately obvious "patentable" use for them. To employ proteins of the instant invention in the identification of signal transduction pathways mediated by the protein-protein interaction using the proteins of the instant invention (see page 24, last 2 lines; page 25, lines 1-10) is clearly to use it as the object of further research which has been determined by the Courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for the claimed protein, then the claimed invention is incomplete and, therefore, does not meet the

requirements of 35 U.S.C. 101 as being useful. Furthermore, because the claimed invention is not supported by a specific asserted utility for the reasons set forth above, credibility cannot be ascertained.

Claims 1-5 are also rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim rejections-35 USC § 112, first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 1-2, 4-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for substantially pure proteins comprising the amino acid sequence as set forth in SEQ ID NO:1 or 2, does not reasonably provide enablement for substantially pure proteins comprising the amino acid sequence as set forth in SEQ ID NO:1 or 2, with upto 50 conservative substitutions or proteins encoded by a nucleic acid that hybridizes under high stringency conditions to a probe the sequence of which consists of SEQ ID NO:3, 59, 75, 78, 79, 80 or 81. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1 and 2 are overly broad in their limitation of "...comprising an amino acid sequence at least 85% identical or 90% identical to SEQ ID NO:1 or 2" and claim 4 is broad because it encompasses muteins with upto 50 conservative amino acid substitutions. No guidance is provided as to which of the myriad of polypeptide species encompassed by the claims will encode a polypeptide with the desired characteristics. With respect to claim 5, the claim encompasses muteins of the polypeptides of SEQ ID NO:1 or 2. Variants of the polypeptide can be generated by deletions, insertions, and substitution, but actual or prophetic examples on expected performance parameters of any of the possible muteins of the protein molecule have not been disclosed. Furthermore, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia,

causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the instant specification as to how one of skill in the art would generate a polypeptide other than that exemplified in SEQ ID NO:1 or 2 of the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Given the breadth of claims 1-2, 4-5, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim rejections-35 USC § 112, second paragraph

4. Claims 1-2, are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "PDZ ~~domain~~ domain sequence" the recitation of which is vague and indefinite because the metes and bounds of this term are unclear.

Claim 2 is rejected as vague and indefinite insofar as it depends on claim 1 for its limitations.

Conclusion

No claim is allowed.

The claims are free of the prior art of record.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
August 15, 2001